UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,633	12/27/2001	Timothy Caspar	BB-1386USPCT	1132

23906 7590 01/30/2004

E I DU PONT DE NEMOURS AND COMPANY
LEGAL PATENT RECORDS CENTER
BARLEY MILL PLAZA 25/1128
4417 LANCASTER PIKE
WILMINGTON, DE 19805

EXAMINER	
BUI, PHUONG T	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,633	CASPAR ET AL.	
	Examiner	Art Unit	
	Phuong T. Bui	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 25-37 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 25-37 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3/1/02.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The Office acknowledges the receipt of Applicant's restriction election filed November 6, 2003. Applicant elects Group I and Invention A (SEQ ID NO:1 encoding SEQ ID NO:2) without traverse. It is noted that the restriction election is unsigned. However, as this appears to be a *bona fide* attempt at a proper response, and in the interest of expediting prosecution, the application is examined on the merits. A signed copy of the restriction election is required. Claims 25-37 are pending and are examined in the instant application. This restriction is made FINAL.

Sequence Listing

2. Applicant's CRF and paper sequence listing have been entered. However, upon examination of SEQ ID NO:1 and its corresponding amino acid sequence SEQ ID NO:2, it is unclear what region of SEQ ID NO:1 encodes SEQ ID NO:2. Clarification is required.

Information Disclosure Statement

3. An initialed and dated copy of Applicant's IDS form 1449, filed March 1, 2002 is attached to the instant Office action.

Drawings

4. Formal drawings are required in response to the instant Office action.

5. The following informality has been noted and requires correction in response to this Office Action. Since figures must be numbered separately, i.e. "Figure 3A," "Figure 3B," etc. , Applicant is required to amend the Brief Description of the Drawings

accordingly to reflect the proper figure designations which are in formal drawings when drawings are submitted.

Claim Rejections - 35 USC § 101 Utility

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 25-37 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility. First of all, Applicant asserted that the nucleotide sequence SEQ ID NO:1 encoding SEQ ID NO:2 has AMP deaminase activity. However, SEQ ID NO:1 does not appear to encode a complete protein, as the first amino acid is not a methionine –a methionine may indicate it is the encoded initiation codon. Applicant does not indicate where the reading frame for SEQ ID NO:1 encoding SEQ ID NO:2 begins or ends (see "Sequence Listing" section above). Applicant provided no evidence that SEQ ID NO:2 has the asserted activity. It is then unclear as to whether SEQ ID NO:1 is only a partial sequence of the AMP deaminase and does not have AMP deaminase activity.

Secondly, Applicant's functional assignment for the encoded protein of SEQ ID NO:2 is based solely upon sequence alignment with a single prior art sequence. Neither Applicant's disclosure nor the state of the prior art at the time the invention was made provides guidance as to where the catalytic domain for Applicant's protein activity is located. Applicant provided no empirical data to verify that SEQ ID NO:1 encodes a polypeptide having AMP deaminase activity, i.e., containing the catalytic domain. In

Table 5 of the specification, Applicant indicates that SEQ ID NO:2 has 42.3% sequence identity to a prior art AMP deaminase protein isolated from human. However, since SEQ ID NO:2 is a partial protein sequence, it is unclear what percent sequence identity the entire protein containing SEQ ID NO:2 would have with the entire protein of the prior art AMP deaminase. It is also unclear that the prior art AMP deaminase used by Applicant for sequence comparison is a complete protein, as such was not disclosed by Applicant. The state of the art to date does not recognize that a 42.3% sequence identity of a partial protein with another protein is sufficient for predicting protein function, especially without any disclosure as to how large the protein is, what size variations exist within the genus of AMP deaminases, whether or not there are highly conserved regions between the different species of AMP deaminases, where the functional domains are, and most importantly, whether or not SEQ ID NO:2 contains all the highly conserved regions and functional domains necessary for AMP deaminase activity. Without such activity, SEQ ID NO:1 or a polynucleotide sequence encoding SEQ ID NO:2 would lack (asserted) utility.

Thirdly, sequence alignment allows one skilled in the art to predict or assign a tentative functional alignment. It does not replace empirical data and is not a verification of a functional activity of a protein. Bork (Genome Research, Vol. 10, 2000, p. 398-400 (U)) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly

automated and accurate (p. 398, col. 1). One of the reasons for this inaccuracy is that the quality of data in public databases is still insufficient. This is particularly true for data relating to protein function. Protein function is context dependent, and both molecular and cellular aspects must be considered (p. 398, col. 2). Conclusions from comparison analyses are often stretched with regard to protein products (p. 398, col. 3). Furthermore, although gene annotation via sequence database searches is already routine, even here the error rate is considerable (p. 399, col. 2). Most features predicted with an accuracy of greater than 70% are of structural nature and, at best, only indirectly imply certain functionality (see p. 399, Table 1 legend). As more sequences are added to databases and as errors accumulate and propagate, it becomes more difficult to infer correct function from the many possibilities revealed by a database search (p. 399, paragraph spanning cols. 2 and 3). Bork cautions that, although current methods seem to capture important features and define general trends, 30% of structure-function features are missing or predicted inaccurately. This must be kept in mind when processing the results (p. 400, paragraph spanning cols. 1 and 2). Moreover, Lazar et al. (Molecular and Cellular Biology, March 1988, Vol. 8, No. 3, p. 1247-1252 (V)) teaches a mutation of aspartic acid 47 and leucine 48 of a transforming growth factor results in different biological activities (Title). Burgess et al. (The Journal of Cell Biology, 1990, Vol. 111, p. 2129-2138 (W)) teaches a single mutation at position 132 from lysine to a glutamic acid residue causes possible dissociation of the heparin-binding and mitogenic activities of heparin-binding (acidic fibroblast) growth factor-1 from its receptor-binding activities (Abstract). Broun et al.

(Science, 13 November 1998, Vol. 282, p. 131-133 (X)) teaches as few as four amino acid substitutions can convert an oleate 12-desaturase to a hydroxylase and as few as six result in conversion of a hydroxylase to a desaturase (Abstract). Based upon the teachings of these references, the state of the art recognizes that a single or very few amino acid differences can alter or ablate protein activity, and a 42.3% sequence identity with a prior art AMP deaminase does not allow one skilled in the art cannot conclude that a partial protein of SEQ ID NO:2 has AMP deaminase activity. While Applicant is not required to provide empirical data to verify the asserted protein activity of Applicant's SEQ ID NO:2, given (a) the fact that SEQ ID NO:1 encodes a partial protein; (b) the lack of verification of AMP deaminase activity for SEQ ID NO:2; (c) the lack of guidance as to whether or not SEQ ID NO:2 possesses the catalytic domain essential AMP deaminase activity; (d) the fact that Applicant used solely sequence alignment to predict function; (e) the 42.3% sequence identity partial protein SEQ ID NO:2 has with the closest prior art AMP deaminase; and (e) the negative teachings of Bork, Lazar, Burgess and Broun above, one skilled in the art cannot reasonably conclude that SEQ ID NO:2 has the asserted AMP deaminase activity or has utility under current utility guidelines.

In addressing claims drawn to a sequence having 85-95% sequence identity at the amino acid level to a nucleotide sequence encoding SEQ ID NO:2, since SEQ ID NO:1 and a polynucleotide encoding SEQ ID NO:2 lack utility for the reasons set forth above, sequences having less than 100% sequence identity would also lack utility.

Applicant should note that no working examples of a sequence having 85-95% sequence identity having AMP deaminase activity are set forth in Applicant's disclosure.

Additionally, there also is no well-established utility for SEQ ID NO:1 and a sequence encoding SEQ ID NO:2. SEQ ID NO:1 does not have a well-established utility for hybridization purposes because the encoded protein does not have utility for the reasons indicated above. Furthermore, a polynucleotide encoding SEQ ID NO:2, (at 85% sequence identity at the amino acid level) would not necessarily hybridize to SEQ ID NO:1 due to codon degeneracy. Thus, for the reasons set forth, the claimed invention lacks utility under current utility guidelines. (see Utility Examination Guidelines published in Federal Register/ Vol. 66, No. 4/ Friday, January 5, 2001/ Notices; p. 1092-1099).

Claim Rejections - 35 USC § 112, first paragraph

7. Claims 25-37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Moreover, the 85-95% sequence identity recitation in the claims encompasses sequences having unspecified deletions, additions, substitutions and combinations thereof while maintaining AMP deaminase activity. It is noted that because SEQ ID NO:2 is a partial protein, it is unclear that SEQ ID NO:2 itself has AMP deaminase activity to begin with. Neither the state of the prior art nor Applicant provided guidance as to which regions of SEQ ID NO:1 or a sequence encoding SEQ ID NO:2 must be retained for activity, and which

regions can tolerate mutations. Applicant provided no working examples of sequences having 85-95% sequence identity. While one skilled in the art can readily make mutations to SEQ ID NO:1 or a sequence encoding SEQ ID NO:2, further guidance is required as to which mutations would be tolerated. Absent of such guidance, one skilled in the art cannot make and use the claimed invention as commensurate in scope with the claims without undue experimentation.

8. Claims 25-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. The claims are drawn to an isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide having at least 85% sequence identity to SEQ ID NO:2. However, the translated amino acid sequence SEQ ID NO:2 is only a partial sequence of a protein (see utility rejection above). SEQ ID NO:1, which encodes SEQ ID NO:2, is only a partial gene sequence and does not encode a complete open reading frame. However, the breadth of the claims reads upon complete gene sequences having in common a nucleotide sequence encoding SEQ ID NO:2. There is insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine the complete structure of a gene encoding an AMP deaminase of *Zea mays*, absent further guidance. Since the claimed genus, i.e, SEQ ID NO:1 or the nucleotide sequence encoding SEQ ID NO:2, encompasses undisclosed genes or genes yet to be discovered, the disclosed structural feature does not constitute a

substantial portion of the claimed genus. Therefore, the disclosure of SEQ ID NO:1, or the nucleotide sequence encoding SEQ ID NO:2, does not provide an adequate description of the claimed genus, and in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of DNAs which comprise the nucleotide sequence encoding SEQ ID NO:2.

Additionally, the claims reciting 85-95% sequence identity lack adequate written description because Applicant does not disclose a representative number of species as encompassed by these claims. The claims encompass mutants and allelic variants and thus imply that structural variants exist in nature, yet no structural variant has been disclosed. The claims also encompass AMP deaminases from other species. The implication is that there is a gene and a protein other than that disclosed which exists in nature, but the structure thereof is not known. Applicant discloses a single sequence SEQ ID NO:1 isolated from corn. Thus, there is insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine such mutants, allelic variants and AMP deaminases from other plants and organisms, absent further guidance. Accordingly, there is lack of adequate description to inform a skilled artisan that applicant was in possession of the claimed invention at the time of filing. See Written Description guidelines published in Federal Register/ Vol.66, No. 4/ Friday, January 5, 2001/ Notices; p. 1099-1111.

Remarks

9. No claim is allowed. It is understood by the Office the recited Clustal V alignment method uses the default parameters set forth on page 24 of the specification. The closest prior art teaches an AMP deaminase isolated from human having 42.3% sequence identity with SEQ ID NO:2 (p. 24 of specification).

10. Papers relating to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Bui whose telephone number is (703) 305-1996.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Phuong Bui
Primary Examiner
Group Art Unit 1638
December 26, 2003

Phuong Bui
PHUONG T. BUI 12/26/03
PRIMARY EXAMINER